RESEARCH ARTICLE

Crystal Structure Analysis of (6-hydroxy-8-(2-hydroxyphenyl)-9-nitro-2, 3, 4, 8-tetrahydro-1H-pyrido [1, 2-a] pyrimidin-7-yl) (1H-indol-3-yl) methanone

K. Hemanathan[1], R. Raja[2], J. Kamlraja[3], K. Sakthi Murugesan[1*]

[1,2]Department of Physics, Presidency College (Autonomous), Chennai-600 005, India

[3]Department of Chemistry, Pondicherry University, Pondicherry-605 014, India

ABSTRACT: Single crystals of (6-hydroxy-8-(2-hydroxyphenyl)-9-nitro-2,3,4,8-tetrahydro-1H-pyrido [1,2-a]pyrimidin-7-yl)(1H-indol-3-yl)methanone. were grown by slow evaporation method and X-ray diffraction analysis reveals monoclinic *C2/c* space group with unit cell dimensions of a = 34.9435(13) Å, b= 8.8855(3) Å, c= 15.0694(6) Å and β= 95.591(1)°. The pyrimidine ring (N3-N4/C12-C15) makes dihedral angle of 68.08(9)° with the phenyl ring (C18-C23). Crystal data were collected using BRUKER SMART APEX II CCD X-ray diffractometer. The structure was solved by direct method and refined on F^2 by full-matrix least-squares procedure to the final R_1 of 0.041 using SHELXL programs.

KEYWORDS: Indol, Pyridin, Crystal packing and crystal structure.

https://doi.org/10.29294/IJASE.5.4.2019.1132-1136

1. INTRODUCTION

Indole is an aromatic heterocyclic group, the parent of a large number of important compounds in nature with significant biological activity [1]. The indole ring system occurs in plants [2] for example, indole-3-acetic acid is a naturally occurring auxin that controls several plant growth activities [3, 4]. Indole derivatives exhibit antibacterial, antifungal [5], antitumor [6], antihepatitis B virus [7] and anti-inflammatory [8] activities. They are also used as bioactive drugs [9] and have also been proven to display high aldose reductase inhibitory [10] and antimicrobial activities [11]. Indole derivatives are also found to possess hypertensive, muscle relaxant and antiviral activities [12]. Some of the indole alkaloids extracted from plants possess interesting cytotoxic and antiphrastic properties.

2. EXPERIMENTAL

2.1 X-Ray Structure Determination

Single crystal of the compound suitable for x-ray diffraction was obtained by slow evaporation method. Three dimensional intensity data were collected on a Bruker [13] SMART APEX CCD Diffractometer using graphite monochromatized Mo-Kα radiation (λ= 0.71073 Å) at Department of chemistry, IIT, Chennai, India. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures using the SHELXL programs [14]. All the non-hydrogen atoms were refined using isotropic and later anisotropic thermal parameters. The hydrogen atoms were included in the structure factor calculation at idealized positions by using a riding model, but not refined. Images were created with ORTEP [15].The crystallographic data for the compound are listed in Table 1.

2.2 Synthesis of the compound

A dried, 10 mL round-bottomed flask was charged with 2-aminoprop-1-ene-1, 1, 3-tricarbonitrile 1 (1.0 mmol), 4-methylbezaldehyde 2 (1.1 mmol), and 2-(nitromethylene) hexahydropyrimidine 3 (1.0 mmol) in EtOH and 10 mol% of piperidine was added to the reaction mixture and heated in an oil bath at reflux for the 5 h. The consumption of the starting material was monitored by TLC. The precipitated solid was filtered and washed with ethanol (2–3 mL), dried under vacuum to obtain pure product in excellent yield (79 %). Finally, the products were recrystallized from EtOH [16].

3. RESULTS AND DISCUSSION

In the title (6-hydroxy-8-(2-hydroxyphenyl)-9-nitro-2,3,4,8-tetrahydro-1H-pyrido [1,2-a]pyrimidin-7-yl)(1H-indol-3-yl) methanone compound with (methylsulfinyl methane(1:1), the pyrimidine ring (N3-N4/C12-C15) inclained with the phenyl ring (C18-C23) system is 68.08(9)°. The dihedral angle between pyridine ring (N3, C10-C11/C15-C17) and phenyl ring (C1-C6) by 85.22(10)° . The oxygen atom deviate from phenyl ring and 1H-pyrido [1,2-a]pyrimidin ring by 0.015 and -0.409Å respectively. In the crystal,

**Corresponding Author: ksakthimurugesan2492@gmail.com*

Received: 05.03.2019 **Accepted:** 18.04.2019 **Published on**: 27.05.2019

molecules are connected by C-H…O, O-H…O and N-H…O hydrogen bonding interactions, which form centro symmetric patterns described by graph-set ring motif $R_2^2(14)$. The packing view of the title compound is shown in fig. (2)

Table 1: 2D Crystal data and structure refinement of the titled compound

Compound	Parameters
Empirical formula	$C_{24}H_{26}N_4O_6S_1$
Formula weight	942.99
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a = 34.9435(13) Å alpha = 90º b = 8.8855(3) Å beta = 95.591º c = 15.0694(6) Å gamma = 90º
Volume	4656.6(3) $Å^3$
Z, Calculated density	2, 1.345 Mg/m^3
F(000)	1976
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	2.699 to 24.996 deg.
Limiting indices	-41<=h<=41, -10<=k<=10, -17<=l<=17.
Reflections collected / unique	30682/ 4091 [R(int) = 0.028]
Completeness to theta = 24.996	99.6%
Max. and min. transmission	0.959 and 0.933
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4091/ 0 / 324
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I)]	R1 = 0.041, wR2 = 0.1182
R indices (all data)	R1 = 0.0492, wR2 = 0.1112

2D- Scheme Structure

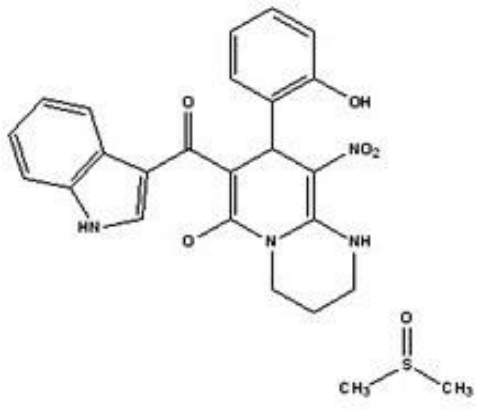


Table 2: Hydrogen-bond geometry [Å]

D—H…A	D—H	H…A	D…A	D—H…A
N2-H2A…O7^{i}	0.865	2.00(2)	2.805(2)	154
N3-H3A…O5^{ii}	0.869	2.297(17)	2.9799(18)	135
O4-H4A…N1^{iii}	0.869	2.590(2)	3.4018(1)	155
C4-H4…O3i^{v}	0.93	2.520(4)	3.237(3)	134

Symmetry code:

i) 2-x,-y, 2-z
ii) x,1-y,1/2+z
iii) x,-y,-1/2+z

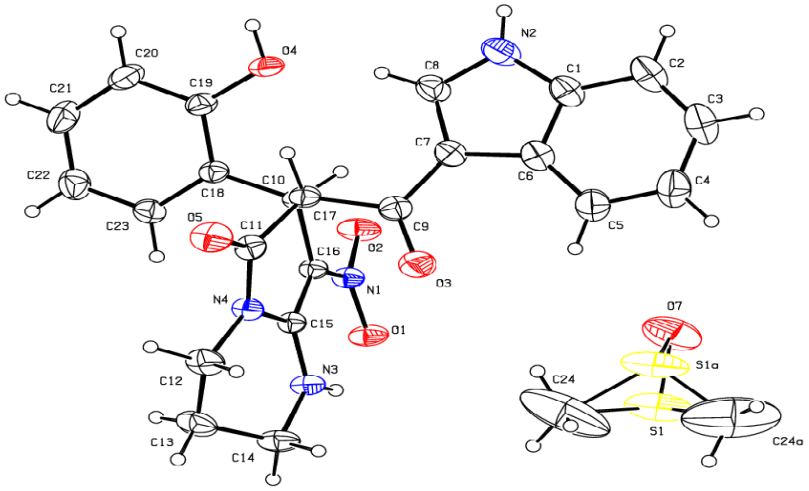
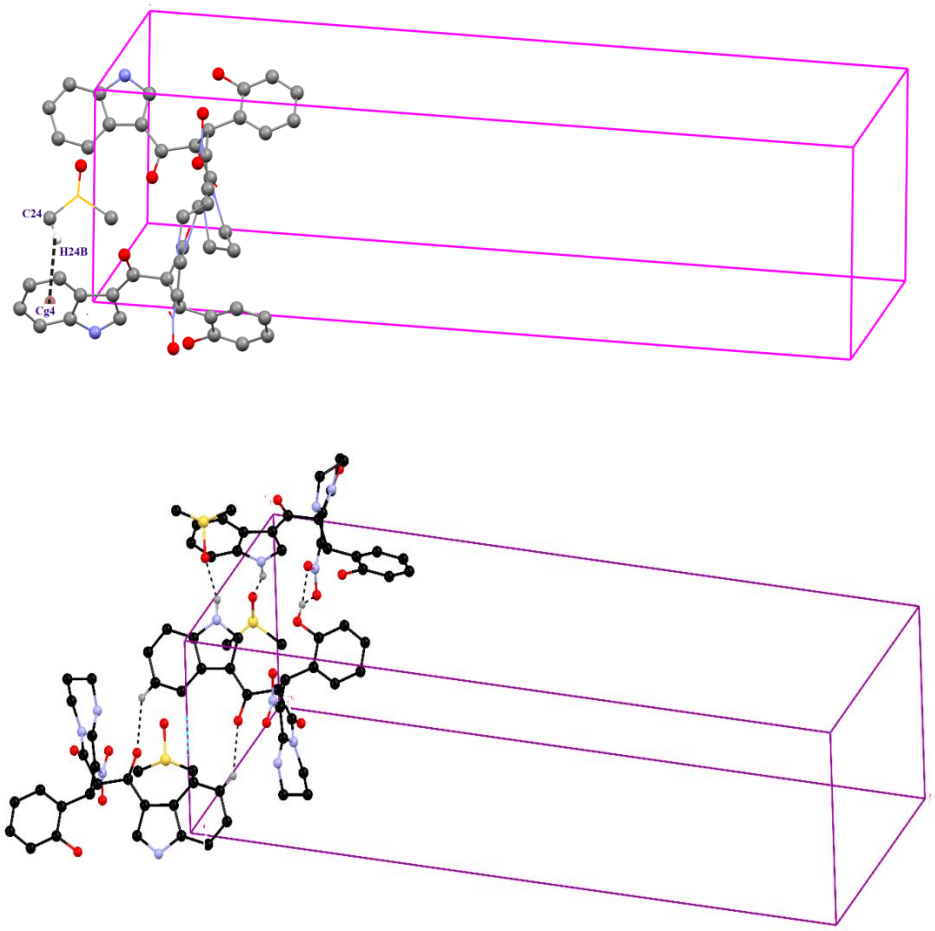


Figure 1 The molecular structure of the title compound with atom labeling. Displacement ellipsoids are drawn at the 30% probability level



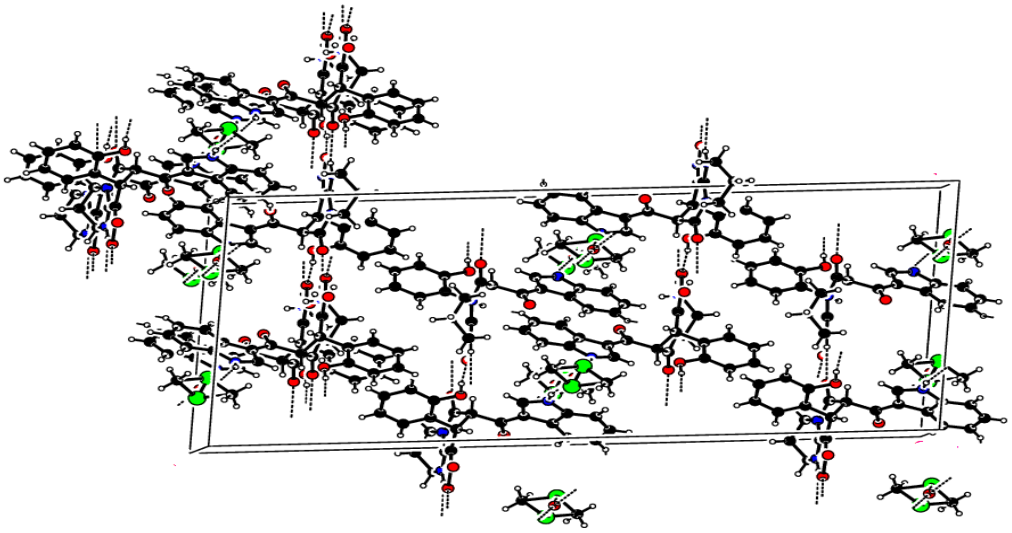


Figure 2 The crystal packing of the titled compound forming C-H…O interactions viewed along b axis. The hydrogen bonds are shown as dashed lines (see Table 2 for details)

Table 3: Selected Some Bond lengths (Å)

Atom	Length	Atom	Length
C1-C2	1.390	C9-O3	1.222
C1-C6	1.395	C14-H14A	0.970
C1-N2	1.382	N1-O1	1.285
C3-H4	0.930	N1-O2	1.248
C6-C7	1.444	O4-H4A	0.870
C8-N2	1.337	S1-C24	1.657

Table 4: Selected Some Bond angles (º)

Atom	Angle	Atom	Angle
C1-C2-C3	117.12	N4-C11-O5	120.36
C2-C1-C6	122.67	C13-C12-N4	111.66
C2-C1-N2	129.59	C18-C19-O4	116.70
C6-C1-N2	107.74	C16-N1-O1	120.75
C3-C4-C5	121.50	O7-S1-C24	107.33
C9-C10-C17	110.92	S1-C24-H24A	109.48

4. CONCLUSION

The crystal structure analysis of a novel indol and pyridin compound was studied using x-ray diffraction method. In the compound, the crystal packing is stabilized by inter and intra molecular hydrogen bonds.

ACKNOWLEDGMENT

The authors thank the Department of Physics (SAIF), IIT, Chennai, India, for X-ray Intensity data collection.

REFERENCES

[1]. Kaushik, N. K., Kaushik, N., Attri, P., Kumar, N., Kim, C. H., Verma, A. K. & Choi, E.H., 2013. Biomedical Importance of Indoles, Molecules, 18, 6620–6662.

[2]. Nigovic, B., Antolic, S., Kojic-Prodic, B., Kiralj, R., Magnus, V. & Salopek-Sondi, B., 2000. Correlation of structural and physico-chemical parameters with the bioactivity of alkylated derivatives of indole-3-acetic acid, a phytohormone (auxin), Acta Crystallographica Section B. 56, 94–111.

[3]. Moore, C. T., 1989. Biochemistry and Physiology of Plant Hormones, ch. 2, p. 33. New Delhi: Narosa Publishing House.

[4]. Fargasova, A., 1994. Bulletin of Environmental Contamination and Toxicology. 52, 706–711.

[5]. Singh, U. P., Sarma, B. K., Mishra, P. K. & Ray, A. B., 2000. Antifungal activity of venenatine, an indole alkaloid isolated from Alstonia venenata. Folia Microbiologica. 45, 173–176.

[6]. Andreani, A., Granaiola, M., Leoni, A., Locatelli, A., Morigi, R., Rambaldi, M., Giorgi, G., Salvani, L. & Garaliene, V., 2001. Synthesis and antitubercular activity of imidazo[2,1-b]thiazoles. Anti-Cancer Drug Design. 16, 167–174.

[7]. Chai, H., Zhao, C. & Gong, P., 2006. Synthesis and in vitro anti-hepatitis B virus activities of some ethyl 6-bromo-5-hydroxy-1*H*-indole-3-carboxylates. Bioorg. Medi. Chem. 14, 911– 917.

[8]. Rodriguez, J. G., Temprano, F., Esteban-Calderon, C., Matrinez- Ripoll,M. & Gracia-Balanco, S., 1985. Conformational and molecular study of the 4-(2-carboxyethyl)-1,2,3,4-tetrahydrocyclopent[b]indole. Tetrahedron, 41, 3813–3823.

[9]. Stevenson, G. I., Smith, A. L., Lewis, S. G., Nedevelil, J. G., Patel, S., Marwood, R. & Castro, J. L., 2000. 2-Aryl tryptamines: selective high-affinity antagonists for the h5-HT2A receptor. Bioorganic & Medicinal Chemistry Letters. 10, 2697–2704.

[10]. Rajeswaran,W. G., Labroo, R. B., Cohen, L. A. & King, M. M., 1999. Synthesis of 5-[(Indol-2-on-3-yl)methyl]-2,2-dimethyl-1,3- dioxane-4,6-diones and Spirocyclopropyloxindole Derivatives. Potential Aldose Reductase Inhibitors**.** Journal of Organic Chemistry. 64, 1369–1371.

[11]. Amal Raj, A ., Raghunathan, R., Sridevikumar, M. R. & Raman, N., 2003. Synthesis, antimicrobial and antifungal activity of a new class of spiro pyrrolidines. Bioorganic & Medicinal Chemistry. 11, 407–419.

[12]. Kolocouris, N., Foscolos, G. B., Kolocouris, A., Marakos, P., Pouli, N., Fytas, G., Ikeda, S. & De Clercq, E., 1994. Synthesis and Antiviral Activity Evaluation of Some Aminoadamantane Derivatives**.** Journal of Medicinal Chemistry. 37, 2896– 2902.

[13]. Bruker (2008). APEX2, SADABS and SAINT. Bruker AXS Inc., Madison,Wisconsin, USA.

[14]. Sheldrick, G. M. (2008). A short history of *SHELX*. Acta Cryst. Section A. 64, 112–122.

[15]. Farrugia, L. J., 2012. Journal of Applied Crystallography. 45, 849–854.

[16]. Hemanathan, K., Raja, R., Kathivelan, D., Reddy, B, S, R, & Sakthi Murugesan, K., 2015. Crystal structure analysis of (2'S,3'S,4'S)-3'-(4-Chloro-2H-chromen-3-yl)-4'-(1H-indole-3-carbonyl)-1'-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-4'-carbonitrile.International Journal of Chem Tech Research. 8(6), 344-348.